

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C. 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 09 August 2000 (09.08.00)	
International application No. PCT/US99/26866	Applicant's or agent's file reference 2026-492PC
International filing date (day/month/year) 12 November 1999 (12.11.99)	Priority date (day/month/year) 09 December 1998 (09.12.98)
Applicant SCHLOM, Jeffrey et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

13 June 2000 (13.06.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Pascal Piriou
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

From the INTERNATIONAL BUREAU

PCT

INFORMATION CONCERNING ELECTED
OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

To:

FEILER, William, S.
Morgan & Finnegan, L.L.P.
345 Park Avenue
New York, NY 10154
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 09 August 2000 (09.08.00)		
Applicant's or agent's file reference 2026-492PC		IMPORTANT INFORMATION
International application No. PCT/US99/26866	International filing date (day/month/year) 12 November 1999 (12.11.99)	Priority date (day/month/year) 09 December 1998 (09.12.98)
Applicant THE GOVERNMENT OF THE UNITED STATES OF AMERICA represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES		

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

AP : GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW
EP : AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
National : AU, BG, BR, CA, CN, CZ, DE, IL, JP, KP, KR, MN, NO, NZ, PL, RO, RU, SE, SK, US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

EA : AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
OA : BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
National : AE, AL, AM, AT, AZ, BA, BB, BY, CH, CR, CU, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IN, IS, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MW, MX, PT, SD, SG, SI, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer: Pascal Pirlou Telephone No. (41-22) 338.83.38
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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

2026-4292 PC

PCT

K. Brown

To:

FEILER, William S.
Morgan & Finnegan, L.L.P.
345 Park Avenue
New York, New York 10154
ETATS-UNIS D'AMERIQUE

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year) 07.03.2001

Applicant's or agent's file reference

2026-4292 PC 4292 PC

IMPORTANT NOTIFICATION

International application No.

PCT/US99/26866

International filing date (day/month/year)

12/11/1999

Priority date (day/month/year)

09/12/1998

Applicant

THE GOVERNMENT OF THE UNITED STATES OF AM...et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
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Authorized officer

Hingel, W

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2026-492PC	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/26866	International filing date (day/month/year) 12/11/1999	Priority date (day/month/year) 09/12/1998	
International Patent Classification (IPC) or national classification and IPC C12N15/86			
Applicant THE GOVERNMENT OF THE UNITED STATES OF AM...et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 13/06/2000	Date of completion of this report 07.03.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Herrmann, K Telephone No. +49 89 2399 2670



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/26866

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*)

Description, pages:

1-112 as originally filed

Claims, No.:

1-106 as originally filed

Drawings, sheets:

1/55-55/55 as originally filed

Sequence listing part of the description, pages:

1-15, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/26866

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:
see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 75-103 (with respect to industrial applicability).

because:

- ☒ the said international application, or the said claims Nos. 75-103 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/26866

1. Statement

Novelty (N)	Yes:	Claims	2, 5, 18, 27, 31, 33, 47, 49, 55, 70-72, 82-88, 105, 106
	No:	Claims	1, 3, 4, 6-17, 19-26, 28-30, 32, 34-46, 48, 50-54, 56-69, 73-81, 89-104
Inventive step (IS)	Yes:	Claims	5, 18, 27, 71, 72
	No:	Claims	1-4, 6-17, 19-26, 28-70, 73-106
Industrial applicability (IA)	Yes:	Claims	1-74, 104-106
	No:	Claims	

2. Citations and explanations **see separate sheet**

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/26866

Citations

The documents mentioned in this International Preliminary Examination Report (IPER) are numbered as in the International Search Report dated 29.03.00, i.e. **D1** and **D4** correspond to the first and the last document of the search report, respectively.

Re ITEM I (Basis of the opinion)

The application as filed contains a sequence listing consisting of 15 pages (41 sequences).

Re ITEM III (Non-establishment of opinion)

Claims 75-103 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT (*in vivo* treatment or diagnostic methods on the human or animal body). Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(i) PCT).

For the assessment of the present claims 75-103 on the question whether they are industrially applicable, no unified criteria exist among the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re ITEM V (Novelty, inventive step, industrial applicability)

1 Summary of the present application

The problem of present application can be seen in the provision of a vector which hyperstimulates T-cells without the induction of apoptosis. This problem has been

solved by providing a poxviral vector containing the three costimulatory molecules B7-1, ICAM-1 and LFA-3.

2 Novelty (Art. 33(2) PCT)

2.1 The subject-matter of claims 2, 5, 18, 27, 31, 33, 47, 49, 55, 70-72, 82-88, 105 and 106 has not been made available to the public by any of the available prior art documents and can therefore be regarded as novel.

2.2 The subject-matter of claims 1, 3, 4, 6-17, 19-26, 28-30, 32, 34-46, 48, 50-54, 56-69, 73-81 and 89-104 does not meet the requirements of Art. 33(2) and 33(3) PCT in view of **D1**.

2.3 **D1** discloses a recombinant vector comprising foreign nucleic acid sequences encoding multiple costimulatory molecules, e.g. B7-1 and B7-2, or functional portions thereof (see **D1**, p. 11, l. 29; p. 12, par. 4; also cf. p. 4, l. 10-13 of present description).

The recombinant vector of **D1** further comprises a foreign nucleic acid sequence encoding at least one cytokine (**D1**, p. 11, l. 28) and promoters derived from e.g. SV40 (**D1**, p. 14, par. 2).

The recombinant vector of **D1** is selected from the group comprising vaccinia virus, fowlpox, virus, MVA, adenovirus, baculovirus and the like (**D1**, p. 13, l. 13-15).

In another embodiment of **D1** tumor associated antigens such as MUC-1, MUC-2 are used (**D1**, p. 15, l. 14-32).

The host cell infected, transfected or induced with the recombinant vector of **D1** is for instance a dendritic cell (**D1**, p. 13, l. 10).

D1 further discloses methods of treatment or prevention of disease in an individual comprising the steps of e.g. present independent claims 89 and 100 (**D1**, p. 7, par. 4; p. 19, penultimate line and p. 2, l. 1-2).

2.4 Furthermore, due to the very open claim language recited in e.g. claim 1 ("functional portions thereof") and claim 4 ("homologs") novelty of said claims is further jeopardized.

3 Inventive step (Art. 33(3) PCT)

- 3.1 The subject-matter of claims 5, 18, 27, 71 and 72 cannot be derived from the available prior art in an obvious manner and therefore complies with the requirements of Art. 33(3) PCT.
- 3.2 The subject-matter of claims 2, 31, 33, 47, 49, 55, 70, 82-88, 105 and 106 does not meet the requirements of Art. 33(3) EPC.
- 3.3 The subject-matter of claims 31, 33, 105 and 106 does not contribute to an inventive solution of an unexpected technical problem. Said claims contain subject-matter which is considered merely an obvious modification to a person skilled in the art.
- 3.4 The IPEA is of the opinion that It was surprising to find that the three costimulatory molecules B7-1, ICAM-1 and LFA-3 induced the activation of T cells to a far greater extent than cells infected with one or two costimulatory molecules or cells infected with three individual constructs, each containing one costimulatory molecule. It was also surprising to find that despite this "hyperstimulation" no evidence of apoptosis was observed (see **D4** (Hodge et al., 15.11.99), abstract, cited as an expert's opinion).
However, e.g. claims 1 and 2 do not exclude a recombinant vector comprising four or more costimulatory molecules ("at least three"). The IPEA is of the opinion that, since it was surprising to find that three costimulatory molecules in one construct will not lead to apoptosis, using four costimulatory molecules will do so. Thus, the problem underlying present application has only been solved by using the **three** costimulatory molecules B7-1, ICAM-1 and LFA-3. Only this technical feature (present claim 5) is regarded as inventive by the IPEA.
Consequently, the subject-matter of claims 2, 47, 49, 55, 70 and 82-88 cannot be regarded as meeting the requirements of Art. 33(3) PCT.

4 Industrial applicability (Art. 33(4) PCT)

Claims 1-74 and 104-106 meet the criteria as set forth by Art. 33(4) PCT.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/26866

Re ITEM VII (Certain defects in the international application)

- 1 Claim 5 is erroneously referring to itself. Claim 5 has been searched and examined as if it were referring to claim 1.
- 2 The present application contains such a high number of independent claims (19 out of 106!) that the application as a whole lacks conciseness (Rule 6.1(a) PCT, also cf. Rule 6.4 PCT). 11 independent claims do not even refer to another claim (e.g. claims 45, 46, 54, 55, 64, 70, 82, 89, 100, 105). Independent claims 1, 64, 70 are all directed to "a vector". The same objection applies mutatis mutandis to independent claims 37, 38, 45, 46, 60 ("a cell"), independent claims 54 and 55 ("a recombinant poxvirus") and claims 75, 82, 89, 94, 95, 100 ("methods of treatment").